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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/889,324      | 07/13/2001  | Shizuo Akira         | 31671-173143        | 2302             |

26694 7590 04/20/2005

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| EXAMINER |
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QIAN, CELINE X

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| ART UNIT | PAPER NUMBER |
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1636

DATE MAILED: 04/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/889,324

Applicant(s)

AKIRA ET AL.

Examiner

Celine X. Qian Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 22 December 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 8,9 and 12-65 is/are pending in the application.
- 4a) Of the above claim(s) 8,9 and 12-51 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 52-55,59-61,64 and 65 is/are allowed.
- 6) ☒ Claim(s) 56-58,62 and 63 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 14 May 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- 1) ☐ Certified copies of the priority documents have been received.
  - 2) ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - 3) ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |                                                                                                                        |                                                                                         |
|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                                                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____                                                |

### **DETAILED ACTION**

Claims 8, 9, 12-65 are pending in the application. Claims 8, 9, 12-51 are withdrawn from consideration for being directed to non-elected subject matter. Claims 52-65 are currently under examination.

This Office Action is in response to the Amendment filed on 12/22/04.

#### ***Response to Amendment***

The rejection of claims 52-55 under 35 U.S.C. 112 1<sup>st</sup> paragraph has been withdrawn in light of Applicant's amendment of the claims.

Claims 56-58 and newly added claims 62-63 stand rejected for reasons set forth of the record mailed on 9/22/04 and further discussed below.

#### ***Response to Arguments***

In response to the scope of enablement rejection set forth in the previous office action, Applicants assert that the amended claims reflect separate phenotype of two knockout mouse in which claims 52-58 are drawn to a mouse having disruption of TLR2, and claims 59-65 are drawn to a mouse having disruption of MyD88. Applicants thus conclude that the claimed inventions are enabled to their full scope.

This argument has been fully considered but deemed unpersuasive with regard to claims 56-58. Although the amended claims separately claim a mouse having disruption in the TLR2 gene and MyD88 gene, the recited phenotypes are same for the two mice (see claims 52-58 and 59-65). As indicated in the previous office action, the phenotype of the two knockout mice may have some overlap, they are not exactly same. The enabled invention is a mouse comprising homozygous disruption of TLR2 gene in its genome, wherein such disruption results in no production of endogenous TLR2 protein,

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and wherein said mouse exhibits the phenotype of being unresponsive to bacterial cell components that is a lipoprotein/lipopeptide, and further unresponsive to peptidylglycan, and hyporesponsive to cell wall fraction of Gram positive bacteria based on the disclosure of the specification. The amended claims 56-58 are drawn to a mouse with disruption of TLR2 gene, and have the phenotype of unresponsive to endotoxin, lipoteichoic acid or mycobacterium tuberculosis lysate. The specification does not disclose such phenotype for the TLR2 knockout mouse. As discussed in the previous office action, the phenotype of the mouse is essential characteristic for the enablement of the claimed mouse. As such, the specification is not enabling for a mouse that has a disruption in the TLR2 gene and exhibits a phenotype that is not disclosed in the specification. Therefore, the claimed invention is not enabled.

Similarly, newly added claims 62 and 63 are drawn to a mouse having a disruption in the MyD88 gene and have the phenotype of hyperresponsive to a cell wall fraction of Gram-positive bacteria or endotoxin. The enabled invention is a mouse comprising homozygous disruption of MyD88 gene in its genome, wherein such disruption results in no production of endogenous MyD88 protein, and wherein said mouse exhibits the phenotype of being unresponsive to bacterial cell components that is a lipoprotein/lipopeptide, and further unresponsive to peptidylglycan, lipoteichoic acid, Mycobacterium tuberculosis lysate, and hyporesponsive to cell wall fraction of Gram negative bacteria based on the disclosure of the specification. The specification does not disclose the claimed phenotype for such mouse. For reasons discussed in the previous office action and above, the specification is not enabling for a mouse having a disruption

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in the MyD88 gene and exhibits a phenotype not disclosed in the specification.

Therefore, the claims are not enabled.

***Conclusion***

Claims 52-55, 59-61, 64 and 65 are allowable.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine X Qian Ph.D.  
Examiner  
Art Unit 1636

**CELIAN QIAN**  
**PATENT EXAMINER**

